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Health Effects Assessment for Polycyclic Aromatic Hydrocarbons (PAHS)

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16. ABSTRACT

This document represents a brief, quantitatively oriented scientific summary of health effects data. It was developed by the Environmental Criteria and Assessment Office to assist the Office of Emergency and Remedial Response in establishing chemical-specific health-related goals of remedial actions. If applicable, chemical-specific subchronic and chronic toxicity interim acceptable intakes are determined for systemic toxicants, or q_1^* values are determined for carcinogens for both oral and inhalation routes.

A q_1^* was determined for polycyclic aromatic hydrocarbons based on both oral and inhalation exposure. These estimates are based on benzo[a]pyrene, the most potent constituent in PAH containing mixtures identified to date. The text provides information concerning the limitations of these estimates.

q(sub1)*

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U.S. Environmental Protection Agency
Office of Research and Development
Office of Health and Environmental Assessment
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Cincinnati, OH 45268

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Office of Solid Waste and Emergency Response
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PREFACE

This report summarizes and evaluates information relevant to a preliminary interim assessment of adverse health effects associated with polycyclic aromatic hydrocarbons. All estimates of acceptable intakes and carcinogenic potency presented in this document should be considered as preliminary and reflect limited resources allocated to this project. Pertinent toxicologic and environmental data were located through on-line literature searches of the Chemical Abstracts, TOXLINE, CANCERLINE and the CHEMFATE/DATALOG data bases. The basic literature searched supporting this document is current up to September, 1984. Secondary sources of information have also been relied upon in the preparation of this report and represent large-scale health assessment efforts that entail extensive peer and Agency review. The following Office of Health and Environmental Assessment (OHEA) sources have been extensively utilized:

U.S. EPA. 1980a. Ambient Water Quality Criteria for Acenaphthene. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-015. NTIS PB 81-117269.

U.S. EPA. 1980b. Ambient Water Quality Criteria for Fluoranthene. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-049. NTIS PB 81-117608.

U.S. EPA. 1980c. Ambient Water Quality Criteria for Polynuclear Aromatic Hydrocarbons. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-069. NTIS PB 81-117806.

U.S. EPA. 1983a. Review of Toxicologic Data in Support of Evaluation for Carcinogenic Potential of: Anthracene. Prepared by the Carcinogen Assessment Group, OHEA, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983b. Review of Toxicologic Data in Support of Evaluation for Carcinogenic Potential of: Benzo[a]anthracene. Prepared by the Carcinogen Assessment Group, OHEA, ORD, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983c. Review of Toxicologic Data in Support of Evaluation for Carcinogenic Potential of: Benzo[a]pyrene. Prepared by the Carcinogen Assessment Group, OHEA, ORD, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983d. Review of Toxicologic Data in Support of Evaluation for Carcinogenic Potential of: Dibenz[a,h]anthracene. Prepared by the Carcinogen Assessment Group, OHEA, ORD, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983e. Review of Toxicologic Data in Support of Evaluation for Carcinogenic Potential of: Fluorene. Prepared by the Carcinogen Assessment Group, OHEA, ORD, Washington, DC for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983f. Reportable Quantity for Acenaphthene. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1983g. Reportable Quantity for Benzo[a]pyrene. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

The intent in these assessments is to suggest acceptable exposure levels whenever sufficient data were available. Values were not derived or larger uncertainty factors were employed when the variable data were limited in scope tending to generate conservative (i.e., protective) estimates. Nevertheless, the interim values presented reflect the relative degree of hazard associated with exposure or risk to the chemical(s) addressed.

Whenever possible, two categories of values have been estimated for systemic toxicants (toxicants for which cancer is not the endpoint of concern). The first, the AIS or acceptable intake subchronic, is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs during a limited time interval (i.e., for an interval that does not constitute a significant portion of the lifespan). This type of exposure estimate has not been extensively used or rigorously defined, as previous risk assessment efforts have been primarily directed towards exposures from toxicants in ambient air or water where lifetime exposure is assumed. Animal data used for AIS estimates generally include exposures with durations of 30-90 days. Subchronic human data are rarely available. Reported exposures are usually from chronic occupational exposure situations or from reports of acute accidental exposure.

The AIC, acceptable intake chronic, is similar in concept to the ADI (acceptable daily intake). It is an estimate of an exposure level that would not be expected to cause adverse effects when exposure occurs for a significant portion of the lifespan [see U.S. EPA (1980d) for a discussion of this concept]. The AIC is route specific and estimates acceptable exposure for a given route with the implicit assumption that exposure by other routes is insignificant.

Composite scores (CSs) for noncarcinogens have also been calculated where data permitted. These values are used for ranking reportable quantities; the methodology for their development is explained in U.S. EPA (1983h).

For compounds for which there is sufficient evidence of carcinogenicity, AIS and AIC values are not derived. For a discussion of risk assessment methodology for carcinogens refer to U.S. EPA (1980d). Since cancer is a process that is not characterized by a threshold, any exposure contributes an increment of risk. Consequently, derivation of AIS and AIC values would be inappropriate. For carcinogens, q_1^*s have been computed based on oral and inhalation data if available.

ABSTRACT

In order to place the risk assessment evaluation in proper context, refer to the preface of this document. The preface outlines limitations applicable to all documents of this series as well as the appropriate interpretation and use of the quantitative estimates presented.

The major issue of the PAH risk assessment is the potential carcinogenicity of these compounds. There are limited data available which can be used for quantitative risk assessment, however, this does not imply that there are not adequate qualitative data to consider many of the members of this class as animal carcinogens. In addition, PAH containing mixtures are documented to contribute to increased incidence of cancer in the human population. The contribution of individual chemical species to the carcinogenic potency of these mixtures and the interactions of various componets cannot be adequately addressed at present.

The one PAH, benzo(a)pyrene, for which adequate dose-response data following exposure by appropriate routes (inhalation, oral) are available has been used to develop a cancer-based risk assessment for PAHs. Since data indicate that benzo(a)pyrene is one of the most potent carcinogens of the PAHs tested, it is suggested that cumulative exposures to mixtures containing PAH concentrations should result in a risk that is less than that predicted for benzo(a)pyrene alone. However, it should be kept in mind that many of the PAHs are still inadequately characterized in terms of their carcinogenic potential; that interactions of constituents of mixtures are poorly defined; and that potency ranking has been done using mouse skin exposure data (data for other routes from which potency comparisons could be made are not available).

Using data for stomach tumors in mice following oral exposure to benzo-(a)pyrene, a q_1^* of 11.53 $(mg/kg/day)^{-1}$ was computed for oral exposure. Similarly, using data on incidence of respiratory tumors in hamsters exposed to benzo(a)pyrene by inhalation exposure, a q_1^* of 6.11 $(mg/kg/day)^{-1}$ was derived.

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LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AIC	Acceptable intake chronic
AIS	Acceptable intake subchronic
BCF	Bioconcentration factor
bw	Body weight
CAS	Chemical Abstract Service
CS	Composite score
GI	Gastrointestinal
NOEL	No-observed-effect level
ppm	Parts per million
TLV	Threshold limit value
TWA	Time-weighted average

1. ENVIRONMENTAL CHEMISTRY AND FATE

Polycyclic aromatic hydrocarbons (PAHs) are a class of compounds that are formed during the incomplete combustion or pyrolysis of organic materials containing carbon and hydrogen. Several hundred different PAHs have been identified from combustion and pyrolysis sources (Grimmer, 1983). In this discussion, only a few PAHs compounds (containing 2-6 aromatic rings) that occur most frequently in the environment (Grimmer, 1983) and also appear on the U.S. EPA's list of priority pollutants will be considered. The relevant physical and chemical properties and CAS Registry numbers of a few selected PAHs are given in Table 1-1.

The half-lives of PAHs in a particular medium are not known with certainty. Based on the available experimental data, some speculation about the half-lives can be made. According to the theoretical predictions of Cupitt (1980) and the experimental work of Yamasaki et al. (1982), the majority of naphthalene, phenanthrene, anthracene, fluoranthene and pyrene should exist in the vapor phase in the atmosphere. On the other hand, benz-[a]anthracene, chrysene, benzo[a]pyrene (BaP) and benzo[ghi]perylene should exist predominantly in the particulate sorbed phase in the atmosphere. The removal of PAHs from the atmosphere can occur through photochemical reactions, chemical reactions (principally with OH radicals, ozone and NO_x) and physical removal mechanisms (wet and dry deposition). The PAHs that exist predominantly in the vapor phase in the atmosphere (e.g., naphthalene, phenanthrene, anthracene, fluoranthene and pyrene) are likely to be removed primarily through direct or indirect photochemical reactions (Atkinson et al., 1984; NAS, 1983; Mabey et al., 1981). The half-life for these compounds in the atmosphere should be <1 day. The primary removal mechanism

TABLE 1-1

Selected Physical and Chemical Properties and CAS Numbers of a Few PAHs

Compound	Molecular Weight	CAS No.	Vapor Pressure (mm Hg)	Water Solubility	log K_{ow}[a]	BCF[b]	Reference
Naphthalene	128.16	91-20-3	0.082 at 25°C	31.7 mg/L at 25°C	3.37	146	Mackay et al., 1980, 1982
Phenanthrene	178.22	85-01-8	6.8×10^{-4} at 20°C	1 mg/kg at 25°C	4.46	1,230	Wise et al., 1981; U.S. EPA, 1980c
Anthracene	178.22	120-12-7	1.95×10^{-4} at 20°C	0.0446 mg/kg at 25°C	4.45	1,210	Wise et al., 1981; Mackay and Shiu, 1977; U.S. EPA, 1980c
Fluoranthene	202.24	206-44-0	5.0×10^{-6} at 25°C	0.206 mg/kg at 25°C	4.90	2,920	Wise et al., 1981; U.S. EPA, 1980c; Mabey et al., 1981
Pyrene	202.24	129-00-0	2.5×10^{-6} at 25°C	0.132 mg/kg at 25°C	4.88	2,800	Mabey et al., 1981; Wise et al., 1981; U.S. EPA, 1980c
Benz[a]anthracene	228.20	56-55-3	101×10^{-7} at 20°C	9.4 µg/kg at 25°C	5.61	11,700	Wise et al., 1981; U.S. EPA, 1980c; Santodonato et al., 1981
Chrysene	228.20	218-01-9	6.3×10^{-7} at 25°C	1.8 µg/kg at 25°C	5.61	11,700	Wise et al., 1981; U.S. EPA, 1980c; Mabey et al., 1981
Benzo[a]pyrene	252.30	50-32-8	5.6×10^{-7} at 25°C	1.2 µg/kg at 25°C	6.06	28,200	Wise et al., 1981; U.S. EPA, 1980c; Mabey et al., 1981
Benzo[g,h,i]perylene	276.30	191-24-2	1.03×10^{-10} at 25°C	0.7 µg/kg at 25°C	6.51	68,200	Wise et al., 1981; U.S. EPA, 1980c; Mabey et al., 1981

[a] K_{ow} = octanol/water partition coefficient

[b] BCF = bioconcentration factor, values estimated from the equation of Veith et al., 1979

for benz[a]anthracene and BaP from the atmosphere is likely to be ozonolysis reactions (NAS, 1983). The expected half-life for this process is likely to be <1 day. It should be remembered that the reactivities of the particulate sorbed portions of the PAHs are strongly dependent on the materials on which these compounds are sorbed (Korfmacher et al., 1980). Depending on the nature of particulate matter, the half-life of particulate-sorbed PAHs may be several days to a few weeks. This increased stability of particulate-sorbed PAHs may permit these compounds to participate in long distance transport. In the absence of any chemical reactions, PAHs may still be removed from the atmosphere by physical removal mechanisms. In the case of BaP, the half-life for dry deposition of particle-sorbed compound has been estimated to be ~5.5 days (Cupitt, 1980).

Data sufficient for assessing the aquatic fate of PAHs are not available in the existing literature. Based on the information currently available (Callahan et al., 1979; Mabey et al., 1981), the following conclusions regarding the aquatic fate of PAHs can be made.

The three likely mechanisms that may be responsible for the removal of PAHs from aquatic media are volatilization, photochemical reactions and microbial degradation. With the exception of naphthalene and other PAHs that have relatively high vapor pressures, volatilization is not likely to be a significant removal mechanism. In the case of naphthalene, both volatilization and adsorption may be quite competitive, with the dominant process being dictated by the aquatic conditions. High stream and wind velocities could enhance volatilization, while high organic carbon content could facilitate sedimentation and the subsequent microbial degradation of particle-sorbed naphthalene.

Photolytic degradation of dissolved PAHs is another mechanism by which PAHs can be removed from aquatic media. However, the sediment-water partition coefficients (Mabey et al., 1981) for most PAHs are such that the major portion of the PAHs are expected to remain in a particulate-sorbed state in water bodies. In view of this, if one considers the light attenuation and scattering in water bodies occurring with increased depth and particulate content, photolysis does not appear to be a significant removal mechanism for PAHs.

The predominant mechanism that is likely to dictate the fate of most PAHs in aquatic media is sorption onto particulate matter and subsequent sedimentation and microbial degradation. Depending on the nature of the PAH and the characteristics of the aquatic medium, the half-life for microbial degradation could range from <1 day to several years. Compounds with ≤ 4 cyclic rings are more amenable to microbial degradation than compounds with >4 cyclic rings.

The predominant mechanism for the removal of PAHs from soils is likely to be microbial degradation. Based on the assumption that the potential for microbial degradation of PAHs is greater in soils than in aquatic systems (Callahan et al., 1979), the half-life of PAHs in soils could range from <1 day to a few years. Considering the soil sorption coefficient (Kenaga and Goring, 1980) and water solubilities, these compounds are not expected to have high mobility in soils. Therefore, significant leaching of these compounds into groundwater is not expected, particularly from soils with higher organic carbon content.

2. ABSORPTION FACTORS IN HUMANS AND EXPERIMENTAL ANIMALS

2.1. ORAL

Few quantitative data are available regarding the oral absorption of PAHs; however, oral absorption of PAHs may be inferred from the demonstrated toxicity of PAHs following oral administration (Smyth et al., 1962; U.S. EPA, 1980c, 1981; Santodonato et al., 1981). Polycyclic aromatic hydrocarbons as a class are highly lipid soluble and it has been proposed that they readily absorbed from the GI tract, primarily by passive diffusion (Rees et al., 1971). In particular, BaP, chrysene. and benz[a]anthracene are reported to be readily transported across the GI mucosa (Rees et al., 1971).

A somewhat different assessment of the oral absorption of PAHs was tendered by Grimmer (1983) who generalized that the mucous layer lining the GI tract may impede absorption. Rats given BaP by gavage in starch solution (100 mg) or in the diet (250 mg) absorbed ~50% of the administered compound (Chang, 1943). Regardless of the type of solvent used, BaP readily penetrates the forestomach epithelium of mice (Chang, 1943). In the glandular stomach, however, the type of solvent used plays a decisive role in absorption of BaP (Ekwall et al., 1951; Setala, 1954). Hydrophilic solvents enhance the absorption of BaP from the glandular stomach, while lipophilic solvents do not modify BaP absorption. Mitchell and Tu (1979) reported that an aqueous suspension of pyrene was poorly absorbed from the gut of male Fischer 344 rats.

2.2. INHALATION

Limited experimental data are available regarding the pulmonary absorption of PAHs; however, pulmonary absorption of PAHs may be inferred from the demonstrated toxicity of PAHs following inhalation exposure (U.S. EPA,

1980c, 1981; Santodonato et al., 1981). As a class, PAHs are highly lipid soluble and capable of passage across epithelial membranes (U.S. EPA, 1980c). Benzo[a]pyrene, and presumably other PAHs, are readily absorbed through the lungs (Kotin et al., 1969; Vainio et al., 1976). Mitchell and Tu (1979) reported rapid pulmonary absorption of a pyrene aerosol (300-500 µg/ℓ of air) by male Fischer 344 rats; widespread tissue distribution was seen after 60 minutes of exposure.

3. TOXICITY IN HUMANS AND EXPERIMENTAL ANIMALS

3.1. SUBCHRONIC

3.1.1. Oral. As reported in the abstract of a Polish study, Knobloch et al. (1969) administered acenaphthylene or acenaphthene orally to rats at a dose level of 0.6 g acenaphthylene/kg bw in olive oil for 40 days or 2 g acenaphthene/kg bw in olive oil for 32 days. Treatment with either compound resulted in considerable body weight loss, unspecified changes in the peripheral blood pattern, changes in renal function, and increased serum aminotransferase activities. In addition, rats exposed to acenaphthene had mild morphological damage to the liver and kidneys, changes consistent with mild bronchitis, and localized inflammation of the peribronchial tissue.

Genetic differences appear to influence the subchronic oral toxicity of BaP in mice. Specifically, the Ah locus, which determines the inducibility of aryl hydrocarbon hydroxylase, plays a major role in determining the oral toxicity of BaP, presumably by influencing the pathways of biotransformation. Robinson et al. (1975) administered BaP in the diet at a level of 120 mg/kg bw to nonresponsive (poorly inducible) AKR/N mice (Ah^d/Ah^d type) and to responsive (markedly inducible) mice (Ah^b/Ah^b type). Nonresponsive mice developed aplastic anemia and died within 4 weeks, whereas responsive mice remained healthy for at least 6 months.

3.1.2. Inhalation. As reported in the abstract of a Russian study, Reshetyuk et al. (1970) observed chronic nonspecific pneumonia in male rats following exposure to acenaphthylene at a concentration of 18 mg/m³ or acenaphthene at 12 mg/m³ for 4 hours/day, 6 days/week, for 5 months. The report did not provide details concerning control animals or experimental protocol (U.S. EPA, 1980c).

3.2. CHRONIC

3.2.1. Oral. The only available chronic oral bioassays for PAHs are investigations of the carcinogenicity of BaP and dibenz[a,h]anthracene (U.S. EPA, 1980c). The lack of appropriate protocols (i.e., nontumor pathology) and detailed reporting of symptoms render these carcinogenicity bioassays inadequate for use in evaluating other endpoints.

3.2.2. Inhalation. Pertinent data regarding the nontumor-related chronic toxicity of PAHs administered by inhalation could not be located in the available literature.

3.3. TERATOGENICITY AND OTHER REPRODUCTIVE EFFECTS

3.3.1. Oral. Rigdon and Rennels (1964) fed female rats a diet containing BaP at a level of 1000 mg/kg (equivalent to 50 mg/kg/day) for up to 3.5 months. Of seven pregnant treated animals, only one dam carried viable fetuses to term, delivering four pups on the 23rd day of pregnancy. Two of the four pups were stillborn, one of which was grossly malformed (not necessarily treatment-related). A third pup was killed for observational purposes and the fourth pup apparently died of starvation 3 days after birth, as the dam did not show any signs of lactation. The authors were not certain if this absence of lactation was treatment-related. At autopsy, four dead fetuses were found in the right uterine horn of a second dam. Signs of toxicity (body weight changes or histopathological changes) were not observed in the treated dams.

In a teratogenicity and reproduction study, Rigdon and Neal (1965) fed male and female mice diets containing BaP at a level of 0, 250, 500 or 1000 mg/kg over various time spans during mating, gestation and post-partum. No apparent reproductive, teratogenic, embryotoxic or fetotoxic effects were observed in the experimental animals.

Mackenzie and Angevine (1981) administered BaP orally at a level of 10 mg/kg bw to CD-1 mice during pregnancy. There was no effect on fetal body weights but a marked and specific reduction of gonadal weight occurred. Also, reduced fertility and reproductive capacity were reported among the offspring. At a level of 40 mg/kg/day, almost complete sterility was observed in both sexes of offspring (Mackenzie and Angevine, 1981).

3.3.2. Inhalation. Pertinent data regarding the teratogenic effects resulting from inhalation exposure to PAHs could not be located in the available literature.

3.4. TOXICANT INTERACTIONS

U.S. EPA (1980c) has extensively described the synergistic and antagonistic interactions among different PAHs and between PAHs and non-PAHs chemicals. Briefly, metabolism of PAHs by the microsomal mixed function oxidase enzyme system yields several types of reactive and potentially carcinogenic intermediates. Chemicals that induce or inhibit this enzyme system alter the patterns of PAHs metabolism and, hence, alter their toxic and carcinogenic properties.

4. CARCINOGENICITY

The carcinogenicity of PAHs has been extensively tested by application to the skin of mice, and been the subject of only limited investigation by other routes of administration. The studies discussed below were previously summarized by U.S. EPA (1983a,b,c,d,e). More complete reviews of the carcinogenicity bioassays of PAHs are presented by IARC (1973, 1983), U.S. EPA (1980a,b,c, 1981) and Santodonato et al. (1981).

4.1. HUMAN DATA

Few case reports are available on the direct carcinogenic effects of PAHs on humans. Cottini and Mazzone (1939) applied a 1% solution of BaP in benzene to small areas of exposed and unexposed skin of 26 patients. Up to 120 daily applications were applied over a 4-month period. Regressive verrucae developed in all of the 26 patients within this time. Although reversible and apparently benign, these changes were thought to represent early stages of neoplastic proliferation. Similar cases of epidermal changes were reported by Rhoads et al. (1954) and Klar (1938) in men accidentally exposed to BaP. Numerous epidemiologic studies of human populations (primarily worker groups) have shown a clear association between exposure to PAHs-containing mixtures (soots, tars, oils, etc.) and increased cancer risk (Santodonato et al., 1981; IARC, 1973, 1983; U.S. EPA, 1981).

4.1.1. Oral. Pertinent data regarding the carcinogenicity of pure PAHs to humans following oral exposure could not be located in the available literature.

4.1.2. Inhalation. Pertinent data regarding the carcinogenicity of pure PAHs to humans following inhalation exposure could not be located in the available literature.

4.2. BIOASSAYS

The carcinogenic properties of certain PAHs compounds have been studied in animals for more than 50 years. The predominance of testing has been done with oral, inhalation exposures, mouse skin assays, implantations and subcutaneous injections.

4.2.1. Oral. Benzo[a]pyrene was administered to mice in the diet at various concentrations to test its carcinogenicity (Neal and Rigdon, 1967; Rigdon and Neal, 1966, 1969). These studies are summarized in Tables 4-1, 4-2 and 4-3. A dose-response relationship was noted for the incidence of stomach tumors (papillomas and carcinomas) in male and female CFW-Swiss mice treated with 1-250 ppm BaP for up to 197 days (Neal and Rigdon, 1967). Stomach tumors were reported in animals treated with 20, 40, 45, 50, 100 and 250 ppm BaP (5/23, 1/40, 4/40, 24/34, 19/23 and 66/73, respectively), while control animals (0/289) and those treated with 1, 10 and 30 ppm BaP (0/25, 0/24 and 0/37, respectively) did not have similar tumors. An increased incidence of lung adenoma and leukemia was noted in mice treated with 250 and 1000 ppm BaP, in addition to the increase in stomach tumors (Rigdon and Neal, 1966, 1969).

There is no evidence that anthracene is an animal carcinogen in studies where administration has been by the oral route. In two studies, Druckrey and Schmahl (1955) and Schmahl and Reiter (unpublished data), there were no reports of any tumor formation caused by the administration of anthracene. No tumors were reported in 31 rats treated with 4.4 g anthracene (total dose) during a 33-month study (Schmahl and Reiter, unpublished). Druckrey and Schmahl (1955) reported no tumors in 28 rats receiving 4.5 g (total dose) anthracene.

TABLE 4-1

Carcinogenicity of Benzo[a]pyrene Administered in the Diet to Male and Female CFW Mice at Levels of 1-250 ppm*

Dose	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
1 ppm (0.48 mg total dose)	110 days	140 days	NR	diet	stomach	papillomas/carcinomas	0/25
10 ppm (4.48 mg total dose)	110 days	140 days	NR	diet	stomach	papillomas/carcinomas	0/24
20 ppm (8.88 mg total dose)	110 days	226 days	NR	diet	stomach	papillomas/carcinomas	5/23
30 ppm (13.32 mg total dose)	110 days	143-177 days	NR	diet	stomach	papillomas/carcinomas	0/37
40 ppm (17.76 mg total dose)	110 days	143-211 days	NR	diet	stomach	papillomas/carcinomas	1/40
45 ppm (19.8 mg total dose)	110 days	141-183 days	NR	diet	stomach	papillomas/carcinomas	4/40
50 ppm (21.4-29.4 mg total dose)	107-197 days	124-219 days	NR	diet	stomach	papillomas/carcinomas	24/34
100 ppm (39.2-48.8 mg total dose)	98-122 days	118-146 days	NR	diet	stomach	papillomas/carcinomas	19/23
250 ppm (70-165 mg total dose)	70-165 days	88-185 days	NR	diet	stomach	papillomas/carcinomas	66/73
0.0 ppm	NA	70-300 days	NA	basal diet only	stomach	papillomas/carcinomas	0/289

*Source: Adapted from Neal and Rigdon, 1967

NA = Not applicable

NR = Not reported

TABLE 4-2

Carcinogenicity of Benzo[a]pyrene Administered in the Diet to Male and Female Swiss Mice at Levels of 250-1000 ppm*

Dose	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
1000 ppm (1 mg/g food)	73-83 days	73-83 days	NR	diet	stomach lung	papilloma/carcinoma adenoma	5/9 7/9
1000 ppm (1 mg/g food)	127-187 days	127-187 days	NR	diet	stomach lung	papilloma/carcinoma adenoma	13/13 3/13
250 ppm (0.25 mg/g food)	72-99 days	72-99 days	NR	diet	stomach lung	papilloma/carcinoma adenoma	12/52 26/52
250 ppm (0.25 mg/g food)	147-196 days	147-196 days	NR	diet	stomach lung	papilloma/carcinoma adenoma	9/13 10/13
0.0 ppm	NA	111-120 days	NA	diet only	stomach lung	papilloma/carcinoma adenoma	2/108 25/108

*Source: Adapted from Ridgon and Neal, 1966

NA - Not applicable

NR - Not reported

TABLE 4-3

Carcinogenicity of Benzo[a]pyrene Administered in the Diet to Male and Female Swiss CFW Mice at a Level of 250 ppm[a]

Dose	Duration of Treatment (days)	Duration of Study (days)	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
250 ppm (0.25 mg/g food)	80-140	80-140	NR	diet	stomach lung hematopoietic system	papilloma/carcinoma adenoma leukemia	69/108 52/108 40/108
0.0 ppm	NA	62-300	NA	diet only	stomach lung hematopoietic system	papilloma/carcinoma adenoma leukemia	2/175[b] 33/151 0/175[b]

[a]Source: Adapted from Ridgon and Neal, 1969

[b]Incidence of tumors in a control group reported previously by Rigdon and Neal (1966)

NA = Not applicable

NR = Not reported

The carcinogenicity of BaP has been investigated in mice following administration by gavage (Klein, 1963). The compound, administered as a 3% solution in Methocel-Aerosol O.T., was given in 0.5 mℓ doses, 3 times/week for 5 weeks. The incidence of lung adenomas and liver hepatomas was elevated in animals terminated at either 444 or 547 days; these tumor incidences are summarized in Table 4-4.

Dibenz[a,h]anthracene was the first pure chemical ever shown to produce tumors in animals. Many early studies showed a carcinogenic effect in animals when dibenz[a,h]anthracene was administered orally, subcutaneously or applied to the skin (IARC, 1973; U.S. EPA, 1980c). Snell and Stewart (1962, 1963) reported on the tumorigenic activity of dibenz[a,h]anthracene after its oral administration in groups of male and female DBA/2 strain mice. An olive oil emulsion containing 0.2 mg/mℓ dibenz[a,h]anthracene was used as a replacement for drinking water. An average daily dose of 0.76 mg dibenz[a,h]anthracene for females and 0.85 mg dibenz[a,h]anthracene for males was determined from fluid consumption volumes. Among the animals surviving at 200 days, 27/27 developed pulmonary adenomatosis, 24/27 developed carcinoma of the lung and 16 had hemangioendotheliomas. Among the surviving females, 12/13 developed mammary carcinomas. Among 29 controls, one case of pulmonary adenomatosis was reported. No other tumors were reported in the control group. These tumor incidences are summarized in Table 4-5.

Chronic administration of fluorene in the diet at levels of 0.05-0.5% did not result in a significantly increased incidence of tumors in rats at any site (Wilson et al., 1947; Morris et al., 1960), but the data in one study (Wilson et al., 1947) was inadequately reported. These studies are summarized in Tables 4-6 and 4-7.

TABLE 4-4

Oral Carcinogenicity Testing of Benz[a]anthracene Administered by Gavage to Male $B6AF_1$ Mice*

Dose or Exposure	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
0.5 mℓ 3% solution	5 weeks, 3 doses/week	444 days	NR	Methocel-Aerosol O.T.	lung liver	adenoma hepatoma	37/39 18/39
0.5 mℓ 0.0% solution	5 weeks, 3 doses/week	441 days	NA	Methocel-Aerosol O.T.	lung liver	adenoma hepatoma	10/38 0/38
0.5 mℓ 3% solution	5 weeks, 3 doses/week	547 days	NR	Methocel-Aerosol O.T.	lung liver	adenoma hepatoma	19/20 20/20
0.5 mℓ 0.0% solution	5 weeks, 3 doses/week	547 days	NA	Methocel-Aerosol O.T.	lung liver	adenoma hepatoma	6/20 2/20

*Source: Adapted from Klein, 1963

NA = Not applicable

NR = Not reported

TABLE 4-5

Oral Carcinogenicity Testing of Dibenz[a,h]anthracene Administered in the Drinking Water to Male and Female DBA/2 Mice[a]

Dose or Exposure	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
0.2 mg/mL (0.76-0.85 mg/day)	258 days	258 days	NR	olive oil emulsion	lung	adenoma	27/27
						carcinoma	24/27
					mammary gland	mixed	12/13[b]
					mesentery/ pancreas/lymph	hemangioendothelioma	16/27
0.0 mg	259 days	289 days	NA	olive oil emulsion only	lung	adenoma	1/35
						carcinoma	0/35
					mammary gland	mixed	0/35
					mesentery/ pancreas/lymph	hemangioendothelioma	0/35
0.48-0.56 mg/day	167 days	167 days	NR	olive oil emulsion only	lung	adenoma	7/19
						carcinoma	15/19
					mammary gland	mixed	3/9[b]
					mesentery/ pancreas/lymph	hemangioendothelioma	6/19

[a]Source: Adapted from Snell and Stewart, 1962, 1963

[b]Incidence of mammary tumors stated for female mice; none occurred in males.

NA = Not applicable

NR = Not reported

TABLE 4-6

Carcinogenicity Testing of Fluorene Administered in the Diet to Female Buffalo Rats[a]

Dose or Exposure	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type	Tumor Incidence
4.6 mg/day[b]	18.1 months (range, 4.1-19.2)	19.0 months (range, 5.1-20.1)	NR	diet, fluorene in corn oil	uterus	fibrosarcoma	1/18
						carcinosarcoma	1/18
					R-E system	granulocytic leukemia	1/18
					pituitary	chromophobe adenoma	4/18
0 mg/day	NA	15.5 months (range, 9.4-19.9)	NA	diet	uterus	adenocarcinoma	1/18
						fibroepithelial polyp	2/18
					adrenals	cortical adenoma	5/18
					pituitary	adenomas	6/18
					inguinal region	fibroma	1/18
4.3 mg/day[b]	6.1 months (range, 5.0-6.2)	10.2 months (range, 8.2-10.7)	NR	diet, fluorene dissolved in propylene glycol	kidney	squamous-cell carcinoma	1/11
					ureter	squamous-cell carcinoma	1/11
0 mg/day	NA	13.9 months (range, 7.8-18.2)	NR	diet	kidney	adenoma	1/18
					pituitary	chromophobe adenoma	2/18
					R-E system	granulocytic leukemia	1/18

[a]Source: Adapted from Morris et al., 1960

[b]Reported daily intake of 0.05% dietary fluorene

NA = Not applicable

NR = Not reported

TABLE 4-7

Carcinogenicity Testing of Fluorene Administered in the Diet to Albino Rats*

Sex	Dose or Exposure	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Effects
NR	0.062-1.0%	104 days	104 days	NR	diet	Organs appeared grossly and histologically normal
NR	0.125, 0.25 or 0.5%	453 days	453 days	NR	diet	Squamous metaplasia of the bronchial epithelium in three rats. One rat on the 0.125% diet showed a small kidney tubular adenoma of a type not seen before in the rat colony.

*Source: Adapted from Wilson et al., 1947

NR = Not reported

4.2.2. Inhalation. Thyssen et al. (1981) exposed groups of 24 hamsters by inhalation to BaP at levels of 2.2, 9.5 or 46.5 mg/m³ for 4.5 hours/day for 10 weeks, and 3 hours/day thereafter, 7 days/week for up to 675 days. This study is summarized in Table 4-8. No treatment-related tumors were observed in animals exposed to 2.2 mg/m³. Animals exposed to 9.5 mg/m³, however, developed tumors of the nasal cavity (12%), larynx (31%), trachea (4%) and pharynx (23%). Hamsters exposed to BaP at a level of 46.5 mg/m³ also developed tumors of the respiratory tract (13/25) and upper digestive tract (14/25). No tumors of these types were seen in control animals (Thyssen et al., 1981).

Intratracheal administration of BaP resulted in an increased incidence of respiratory tract neoplasms in both sexes of Syrian hamsters (Ketkar et al., 1978; Feron and Kruysse, 1978). These studies are summarized in Tables 4-9 and 4-10. A dose-related response was reported for hamsters treated with 18.2 and 36.4 mg/animal (total dose) for 52 weeks, followed by a 29-week latency period. The incidence of tracheal papillomas and carcinomas collectively with lung adenomas was 4/29 and 3/27 for low-dose males and females, respectively, and 19/30 and 7/24 for high-dose males and females, respectively (Feron and Kruysse, 1978). Ketkar et al. (1978) reported a high dose-related mortality in hamsters treated at dose levels higher than those used by Feron and Kruysse (1978). Mean survival times ranged from 40 weeks for male hamsters treated with 0.1 mg BaP/week to 10 weeks for males treated with 1.0 mg BaP/week. An increase in the incidence of respiratory tract carcinoma, adenoma and papilloma was reported in treatment groups for both males and females, but a definite dose-related response was not evident (Ketkar et al., 1978).

TABLE 4-8

Carcinogenicity of Benzo[a]pyrene to Male Syrian Golden Hamsters Via Inhalation[a,b]

Dose	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type[c]	Tumor Incidence
2.2 mg/m³ (29 mg total dose)	95.2 weeks	95.2 weeks	NR	NaCl vapor in air	respiratory tract upper digestive tract	tumors tumors	0/27 0/27
9.5 mg/m³ (127 mg total dose)	96.4 weeks	96.4 weeks	NR	NaCl vapor in air	respiratory tract upper digestive tract	tumors tumors	9/26[d] 7/26[d]
46.5 mg/m³ (383 mg total dose)	59.5 weeks	59.5 weeks	NR	NaCl vapor in air	respiratory tract upper digestive tract	tumors tumors	13/25[e] 14/25[e]
0.0 mg/m³	NA	96.4 weeks	NA	NaCl vapor only	respiratory tract upper digestive tract	tumors tumors	0/27 0/27

[a]Source: Adapted from Thyssen et al., 1981

[b]Exposure was for 4.5 hours/day for the first 10 weeks, 3 hours/day thereafter for 7 days/week.

[c]Tumors were papillomas, papillary polyps, and squamous cell carcinomas.

[d]3 nasal cavity, 8 laryngeal, 1 tracheal, 6 pharyngeal and 1 forestomach tumors

[e]1 nasal cavity, 13 laryngeal, 3 tracheal, 14 pharyngeal, 2 esophageal and 1 forestomach tumor

NA = Not applicable

NR = Not reported

TABLE 4-9

Carcinogenicity of Benzo[a]pyrene in Syrian Hamsters Following Intratracheal Administration of 0.10-1.0 mg/week[a]

Sex	Dose	Duration of Treatment[b]	Duration of Study[b]	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type[c]	Tumor Incidence
M	0.10 mg/week	40 weeks	40 weeks	97%	bovine albumin	respiratory tract	various neoplasms	5/25
F	0.10 mg/week	34 weeks	34 weeks	97%	bovine albumin	respiratory tract	various neoplasms	12/30
M	0.33 mg/week	24 weeks	24 weeks	97%	bovine albumin	respiratory tract	various neoplasms	7/29
F	0.33 mg/week	28 weeks	28 weeks	97%	bovine albumin	respiratory tract	various neoplasms	10/28
M	1.0 mg/week	10 weeks	10 weeks	97%	bovine albumin	respiratory tract	various neoplasms	6/27
F	1.0 mg/week	15 weeks	15 weeks	97%	bovine albumin	respiratory tract	various neoplasms	6/30
M	0.0 mg/week	41 weeks	41 weeks	NA	bovine albumin only	respiratory tract	various neoplasms	0/29
F	0.0 mg/week	35 weeks	35 weeks	NA	bovine albumin only	respiratory tract	various neoplasms	0/30

[a]Source: Adapted from Ketkar et al., 1978

[b]Mean Survival Time

[c]Carcinomas, adenomas, adenocarcinomas and papillomas were reported.

NA - Not applicable

TABLE 4-10

Carcinogenicity of Benzo[a]pyrene in Syrian Golden Hamsters Following Intratracheal Administration of 18.2-36.4 mg/animal[a]

Sex	Dose	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tumor Type[b]	Tumor Incidence
M	18.2 mg/hamster total dose	52 weeks (1 dose/week)	81 weeks	>99%	0.9% NaCl	respiratory tract	various	4/29
M	36.4 mg/hamster total dose	52 weeks (1 dose/week)	81 weeks	>99%	0.9% NaCl	respiratory tract	various	19/30
M	0.0 mg/hamster total dose	52 weeks (1 dose/week)	81 weeks	>99%	saline vehicle only	respiratory tract	various	0/30[c]
F	18.2 mg/hamster total dose	52 weeks (1 dose/week)	81 weeks	>99%	0.9% NaCl	respiratory tract	various	3/27
F	36.4 mg/hamster total dose	52 weeks (1 dose/week)	81 weeks	>99%	0.9% NaCl	respiratory tract	various	7/24
F	0.0 mg/hamster total dose	52 weeks (1 dose/week)	81 weeks	>99%	saline vehicle only	respiratory tract	various	0/28[c]

[a]Source: Adapted from Feron and Kruysse, 1978

[b]Papillomas and carcinomas of the trachea and pulmonary ademonas were most prevalent.

[c]Combined tumor incidence of untreated and vehicle controls.

In a study by Stanton et al. (1972), 0.5 mg anthracene in 0.05 mℓ warm soft 1:1 wax-tricaprylin was implanted in the lung by a thoracotomy in Osborne-Mendel female rats (3-6 months old). No epidermal carcinomas were reported in the 55-week study; however, there was a granulomatous reaction in all of the 37 examined animals. No tumors were seen in 10 control animals. This study is summarized in Table 4-11.

4.2.3. Mouse Skin Assays. Many of the polycyclic aromatics produce tumors in mouse skin when applied topically alone or in combination with a promotor. As a result of the route of administration, these studies have limited utility for quantitative risk assessment. However, they provide useful qualitative data which can be used to estimate relative potency. U.S. EPA (1982) has used skin painting data on five PAHs [dibenzo(a,h)-anthracene; benzo(a)anthracene, indeno(1,2,3-c,d)pyrene; chrysene; benzo(b)-fluoranthene] tested using similar protocols to qualitatively compare their potency to BaP. The overall ranking was as follows: BaP $\geq$ DBA > BbF > BaA $\geq$ IP $\geq$ chrysene. This type of analysis becomes especially important when risk assessment estimates for PAHs as a class are attempted. In addition to these compounds which were tested using similar protocols (anthanthrene), benzo(j)fluranthene, 7,12-dimethylbenze(a)anthracene, dibenzo(a,b)pyrene, dibenzo(a,e)pyrene, dibenzo(a,h)pyrene, dibenzo(a,i)pyrene have all been shown to have some degree of carcinogenic activity when tested in mouse skin (CRC, 1983) using various protocols (IARC, 1973).

In addition, PAHs containing mixtures have been found to show carcinogenic acitivity in mouse skin including: crude coal tar, blast furnace tar, soot extracts, oil shale extracts, cigarette smoke condensates, petroleum pitch, automobile exhaust (CRC, 1983; IARC, 1973).

TABLE 4-11

Carcinogenicity Testing of Anthracene in Female Osborne-Mendel Rats by Lung Implantation*

Dose or Exposure	Duration of Treatment	Duration of Study	Purity of Compound	Vehicle or Physical State	Target Organ	Tymor Type	Tumor Incidence
0.5 mg	single implant	55 weeks	refined recrystallized	1:1 wax-tricaprylin	trachea	epidermoid carcinoma	0/37
0.10 mL vehicle	single implant	81 weeks	NA	1:1 wax-tricaprylin	trachea	epidermoid carcinoma	0/10

*Source: Adapted from Stanton et al., 1972

NA = Not applicable

4.2.4. PAH Containing Mixtures. A number of occupational exposure situations involving PAH containing mixtures have been linked to increased incidence of cancer in exposed humans. Exposure of chimney sweeps to soot and coal tar has been associated with increased scrotal cancer. Increased incidence of bronchial carcinoma has been noted in gasworkers and coking workers (CRC, 1983); increased skin cancer in workers in the coal tar and pitch industry (IARC, 1973). Soots, coal-tars, creosote oils, shale oils and cutting oils have been shown to be carcinogenic in animals following skin painting or subcutaneous injection (IARC, 1973). Diesel exhaust condensate and gasoline engine exhaust condensate have been shown to cause skin tumors when topically applied to mice (CRC, 1983).

4.3. OTHER RELEVANT DATA

A large number of short-term genotoxicity tests have been performed with PAHs. Qualitative indications of selected PAHs genotoxicity are summarized in Table 4-12. Many of the PAHs that have shown positive results in one or more in vitro genotoxicity screening tests have given negative results in animal bioassays (Santodonato et al., 1981; IARC, 1973, 1983; U.S. EPA, 1981).

4.4. WEIGHT OF EVIDENCE

Certain PAHs have demonstrated a carcinogenic response by various routes, while others are considered to be noncarcinogenic or have not been tested extensively.

TABLE 4-12

Genotoxicity of Selected PAH[a]

PAH	Positive Result in at Least One Genotoxicity Assay
Anthanthrene	+
Anthracene	+[b]
Benz[c]acridine	+
Benz[a]anthracene	+[b]
Benzo[b]fluoranthene	+[b]
Benzo[b]fluorene	+
Benzo[g,h,i]perylene	+
Benzo[a]pyrene	+[b]
Benzo[e]pyrene	+
Carbazole	-
Chrysene	+[b]
Coronene	+
Cyclopenta[c,d]pyrene	+
Dibenz[a,h]acridine	+
Dibenz[a,j]acridine	+
Dibenz[a,c]anthracene	+
Dibenz[a,h]anthracene	+[b]
7H-Dibenzo[c,g]carbazole	-
Dibenz[a,h]pyrene	+
Dibenzo[a,i]pyrene	+
1,4-Dimethylphenanthrene	+
Fluoranthene	+
Fluorene	+[c]
1-Methylphenanthrene	+
Perylene	+
Phenanthrene	+
Pyrene	+
Triphenylene	+

[a]Source: Adapted from IARC, 1983

[b]Positive for carcinogenicity in at least one animal bioassay

[c]Negative for carcinogenicity in rats fed fluorene in the diet

IARC (1983) has evaluated selected PAHs based on the overall weight of evidence of carcinogenicity to humans. These classifications range from Group 2A (BaP) and 2B meaning that the compound is probably carcinogenic in humans to Group 3 which indicates that there is only limited animal evidence or a paucity of evidence such that the data base is inadequate to assess the human carcinogenic potential. Some of these classifications are based on routes of exposure other than oral and inhalation. As a class, PAH-containing soots, tars and oils are most appropriately classified as Group 1 (IARC, 1983). Applying the criteria proposed by the Carcinogen Assessment Group of the U.S. EPA (Federal Register, 1984) for evaluating the overall weight of evidence for human carcinogenicity, these chemicals are most appropriately classified in Group A.

IARC has judged the following specific PAHs to be probably carcinogenic in humans, there being sufficient animal evidence and or limited human evidence. The corresponding U.S. EPA grouping (Federal Register, 1984) would be Group B1 or B2, depending on the quality of the evidence.

1. benz[a]anthracene
2. benzo[b]fluoranthene
3. benzo[j]fluoranthene
4. benzo[k]fluoranthene
5. benzo[a]pyrene
6. dibenz[a,h]acridine
7. dibenz[a,j]acridine
8. dibenz[a,h]anthracene
9. 7H-dibenzo[c,g]carbazole
10. dibenzo[a,e]pyrene
11. dibenzo[a,h]pyrene
12. dibenzo[a,i]pyrene
13. dibenzo[a,l]pyrene
14. indeno[1,2,3-cd]pyrene

Further, the following compounds have limited animal evidence for carcinogenicity, however, the evidence according to IARC is inadequate for making a definitive statement about the human carcinogenic potential. The appropriate U.S. EPA classification (Federal Register, 1984) for these chemicals is Group C-Possible Human Carcinogen.

1. anthanthrene
2. benz[c]acridine
3. carbazole
4. chrysene
5. cyclopenta[c,d]pyrene
6. dibenz[a,c]anthracene
7. dibenz[a,j]anthracene
8. dibenzo[a,e]fluoranthene
9. 2 and 3-methylfluoranthenes

5. REGULATORY STANDARDS AND CRITERIA

Exposure criteria and TLVs have been developed for PAHs as a class, as well as for several individual PAHs. The U.S. Occupational Safety and Health Administration (OSHA) has set an 8-hour TWA concentration limit of 0.2 mg/m³ for the benzene-soluble fraction of coal tar pitch volatiles (anthracene, BaP, phenanthrene, acridine, chrysene, pyrene) (Code of Federal Regulations, 1981). NIOSH (1977) recommends a concentration limit for coal tar, coal tar pitch, creosote and mixtures of these substances at 0.1 mg/m³ of the cyclohexane-extractable fraction of the sample, determined as a 10-hour TWA. NIOSH (1977) concluded that these specific coal tar products, as well as coke oven emissions, are carcinogenic and can increase the risk of lung and skin cancer in workers. NIOSH (1977) also recommends a ceiling limit for exposure to asphalt fumes of 5 mg airborne particulates/m³ of air.

Environmental quality criteria for PAHs have been recommended for ambient water, which specify concentration limits intended to protect humans against adverse health effects. The U.S. EPA (1980c) has recommended a concentration limit of 28 mg/ℓ for the sum of all carcinogenic PAHs in ambient water. This value is based on a mathematical extrapolation of the results from studies with mice treated orally with BaP, and acknowledges the conservative assumption that all carcinogenic PAHs are equal in potency to BaP. Daily consumption of water containing 28 mg/ℓ of carcinogenic PAHs over an entire lifetime is estimated, on the basis of the animal bioassay data, to keep the lifetime risk of cancer development below one chance in 100,000.

The U.S. EPA has not recommended an ambient water quality criterion for noncarcinogenic PAHs as a class. U.S. EPA (1980b) has recommended, however, an ambient water quality criterion for fluoranthene of 42 µg/ℓ, which is based on the extrapolation of results from chronic toxicity tests in mice that received fluoranthene by repeated application to the skin. In deriving this criterion for fluoranthene, the U.S. EPA (1980b) acknowledged that data suitable for quantitative risk assessment of noncarcinogenic PAHs are essentially nonexistent. An ambient water quality criterion of 0.02 mg/ℓ for acenaphthene has been recommended by the U.S. EPA (1980a) on the basis of organoleptic properties.

6. RISK ASSESSMENT

6.1. ACCEPTABLE INTAKE SUBCHRONIC (AIS)

Some individual PAHs have been shown to be carcinogenic in humans and others to be carcinogenic to animals. Data are available regarding BaP from which carcinogenic potency can be estimated. It is inappropriate, therefore, to calculate an AIS for these chemicals.

6.2. ACCEPTABLE INTAKE CHRONIC (AIC)

Some individual PAHs have been shown to be carcinogenic in humans and others to be carcinogenic to animals. Data are available regarding BaP from which carcinogenic potency can be estimated. It is inappropriate, therefore, to calculate an AIC for these chemicals.

6.3. CARCINOGENIC POTENCY (q_1^*)

A unit risk for carcinogenicity is presented on the basis that an assumption (risk management decision) is made to consider PAHs carcinogenic to humans as a class of compounds or that individual compounds are carcinogens for humans. This assumption (decision) must be made prior to the use of the unit risk value. Because of the relative paucity of PAHs data that is useful for potency estimation, the estimation of the unit risk is based upon the data from a single PAH compound, BaP.

As U.S. EPA (1982) states, on the basis of currently available data, if the cumulative PAHs exposure is less than or equal to the criterion for BaP the resultant risk should be $<10^{-5}$. If the cumulative exposure to other PAHs exceeds the criterion level recommended for BaP, the resultant risk may exceed 10^{-5}. It should be stated that this approach to risk assessment ignores the possibility of carcinogenic synergism of PAHs. Practically, however, it seems likely that the potential for synergism is far outweighed by the difference in carcinogenic potency between BaP and other PAHs.

Exposure to any single PAH compound in occupational or envronmental situations is unlikely to occur. Exposures are expected to be to complex mixtures with varying PAH constituents. Little is known at present concerning potential interaction of components in these complex mixtures.

6.3.1. Oral. To protect for carcinogenic effects of all PAHs, a carcinogenic potency factor for humans, q_1^*, can be derived from the study of Neal and Rigdon (1967), in which BaP at dose levels of 1-250 ppm in the diet was fed to strain CFW mice for ~110 days. This approach to criterion derivations adopts the conservative assumption that all carcinogenic PAHs are equal in potency to BaP. The incidences of stomach tumors (mostly squamous-cell papillomas but some carcinomas) were 0/289 for controls, 0/25 at the 1 ppm (0.13 mg/kg/day) level, 0/24 at 10 ppm (1.3 mg/kg/day), 1/23 at 20 ppm (2.6 mg/kg/day), 0/37 at 30 ppm (3.9 mg/kg/day), 1/40 at 40 ppm (5.2 mg/kg/day), 4/40 at 45 ppm (5.85 mg/kg/day), 24/34 at 50 ppm (6.5 mg/kg/day), 19/23 at 100 ppm (13.0 mg/kg/day) and 66/73 at 250 ppm (32.5 mg/kg/day). U.S. EPA (1980c) used these incidences of stomach tumors to derive a q_1^* of 11.53 $(mg/kg/day)^{-1}$, using the multistage model of Crump adopted by the U.S. EPA (Federal Register, 1980) for computation of carcinogenic potency. The data base from which this q_1^* was derived is presented in Appendix B.

6.3.2. Inhalation. Adopting the same conservative approach as taken above for oral exposure to carcinogenic PAHs, a carcinogenic potency factor for humans, q_1^*, can be derived from the study of Thyssen et al. (1981), in which Syrian golden hamsters were exposed to BaP by inhalation. These animals were exposed at levels of 0, 2.2, 9.5 or 46.5 mg/m^3 for 59.5-96.4 weeks. The incidences of respiratory tumors were 0/27 for controls, 0/27 for the low-dose group, 9/26 for the mid-dose group, and 13/25 for the high-dose group. Because of early mortality in the highest dose group, these

data were excluded from the q_1^* derivation. Based on the respiratory tumor response of male hamsters, and using the linearized multistage model adopted by the U.S. EPA (Federal Register, 1980), a carcinogenic potency factor (q_1^*) of 6.11 $(mg/kg/day)^{-1}$ can be derived for humans. The corresponding dose associated with an increased lifetime cancer risk of 10^{-5} is 2.339×10^{-6} mg/kg/day or 1.64×10^{-4} mg/day for a 70 kg human. Complete data for derivation of the q_1^* are presented in Appendix C.

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APPENDIX A

Summary Table for PAH

Carcinogenic Potency	Species	Experimental Dose/Exposure	Effect	Unit Risk or q_1^*	Reference
Inhalation	hamsters	2.2-9.5 mg/m³	respiratory tract tumors	6.11 $(mg/kg/day)^{-1}$[a,b]	Thyssen et al., 1981
Oral	mice	1-250 ppm	stomach tumors	11.53 $(mg/kg/day)^{-1}$[a,b]	Neal and Rigdon, 1967' U.S. EPA, 1980c

[a]Uses carcinogenic potency of benzo(a)pyrene

[b]These values require that an explicit decision be made which assumes that the compound or compounds are likely to be human carcinogens irrespective of the scientific uncertainty if any, regarding this assumption.

APPENDIX B

Cancer Data Sheet for Derivation of q_1^*

Compound: Benzo[a]pyrene

Reference: Neal and Rigdon, 1967

Species, strain, sex: mice, CFW, male and female

Body weight: 0.034 kg (assumed)

Length of exposure (le) = 110 days

Length of experiment (Le) = 183 days

Lifespan of animal (L) = 630 days

Tumor site and type: stomach, squamous cell carcinomas and papillomas

Route, vehicle: oral, diet

Experimental Doses or Exposures (ppm)	Input	
	Transformed Dose (mg/kg/day)	Incidence No. Responding/No. Tested (or Examined)
0	0	0/289
1	0.13	0/25
10	1.3	0/24
20	2.6	1/23
30	3.9	0/37
40	5.2	1/40
45	5.85	4/40
50	6.5	24/34*
100	13.0	19/23*
250	32.5	66/73*

*These data not used because of lack of fit to multistage model.

APPENDIX C

Cancer Data Sheet for Derivation of q_1^*

Compound: Benzo[a]pyrene

Reference: Thyssen et al., 1981

Species, strain, sex: hamsters/Syrian golden/male

Body weight: 0.12 kg (assumed)

Length of exposure (le) = 666.4 days for lower dose and 674.8 days for higher dose and controls

Length of experiment (Le) = 666.4 days for lower dose and 674.8 days for higher dose and controls

Lifespan of animal (L) = 666.4 days for lower dose and 674.8 days for higher dose and controls

Tumor site and type: respiratory tract/papillomas, papillary polyps and squamous-cell carcinomas

Route, vehicle: inhalation/NaCl vapor in air

	Input	
Experimental Doses or Exposures	Transformed Dose (mg/kg/day)	Incidence No. Responding/No. Tested (or Examined)
0 mg/m³	0	0/27
2.2 mg/m³	0.0892	0/27
9.5 mg/m³	0.385	9/26

See conversions on following page

CONVERSIONS

$$0\ mg/m^3 = 0\ mg/kg/day$$

$$2.2\ mg/m^3 \times \left[\left(\frac{10\ weeks}{95.2\ weeks} \times \frac{4.5\ hours}{24\ hours}\right) + \left(\frac{85.2\ weeks}{95.2\ weeks} \times \frac{3\ hours}{24\ hours}\right)\right] \times \frac{7\ days}{7\ days} \times$$

$$0.037\ m^3/day \div 0.12\ kg \times \frac{666.4\ days}{666.4\ days} \times \left(\frac{666.4\ days}{666.4\ days}\right) 3 = 0.0892\ mg/kg/day$$

$$9.5\ mg/m^3 \times \left[\frac{10\ weeks}{96.4\ weeks} \times \frac{4.5\ hours}{24\ hours}\right) + \left(\frac{86.4\ weeks}{96.4\ weeks} \times \frac{3\ hours}{24\ hours}\right)] \quad \frac{7\ days}{7\ days} \times$$

$$0.037\ m^3/day \div 0.12\ kg \times \frac{674.8\ days}{674.8\ days} \times \left(\frac{674.8\ days}{674.8\ days}\right) 3 = 0.385\ mg/kg/day$$